An ISO 25 PTL Accredited Laboratory

PHILIP MORRIS U.S.A.

INTEROFFICE CORRESPONDENCE

Richmond, Virginia

To: PTL Steering Team **Date:** November 24, 1998

From: Data Review & Approval Guidelines Team (C. Boswell, R. Holleman, S. Hughes, D. Johnson, S. Laffoon, M. Payne, B. Ward)

Subject: **Recommendations for Data Review & Approval Guidelines**

On 9/22/98, the Data Review & Approval Guidelines Team was chartered. The deliverables were to define and document the scope of responsibilities and criteria for reviewing test results, rejecting test results, performing rechecks, and documenting data rejection. These functions were to be reviewed for the testing technicians, laboratory technical leaders, and receiving and reporting analysts (attachment 1). The team consisted of Cindy Boswell (leader), Robin Holleman, Saundra Hughes, Doris Johnson, Susan Laffoon, Barbara Ward, and Martha Payne, with Wade Mokarry as the sponsor (replacing Becky Tobey). The following is a review of our recommendations, presented on 11/4/98.

Focus Statements

The main function of the Product Testing Laboratory is to provide our collaborators with accurate and timely data that assist them in making decisions about our products. Therefore, we want to focus on the integrity of our data, so that others can ensure the integrity of our products. The statements on attachment 2 served to keep us focused on the main function at each of the levels of data review and approval under consideration.

Team Process

The team met approximately 13 times between September 22 and November 3, 1998. We began by reviewing the current data review and approval processes for each lab area, by test or group of tests, and identified guidelines that were in place. We identified guidelines that were, in our opinion, subjective, inconsistent, or questionable; guidelines that could be improved and streamlined; and areas for which no guidelines existed. After the identified issues were categorized and addressed, recommendations were developed. Attachments 3 through 5 illustrate the accountabilities and recommendations for each of the three levels under consideration.

Testing Technicians

For the testing technicians to ensure the correct and consistent calibration and testing based on procedures, work instructions, checklists, and control charts, we recommend that work instructions be at all stations. For this to occur, we recommend that Natural Management Teams within each laboratory ensure that all test instructions are correct, usable, and posted at the test stations. Natural Management Teams may charter laboratory sub-teams to accomplish this. In addition, we recommend that control chart guidelines be developed by a sub-team so that testing

DOC CODE: P0622

technicians will know how to detect control chart alarms and the procedures to follow when they are detected. Some guidelines may be laboratory-specific.

For the testing technicians to help ensure that samples are not mixed up, we recommend that they make certain that the correct sample is tested. At present, there is no way for this to occur because only sample codes, which are difficult to decipher, appear on the barcodes. We recommend that IS be requested to modify barcodes and groupsheets so that brand names can appear for technicians to compare their samples to the paperwork. We also recommend that the testing technicians ensure all associated analyses are requested for the samples as per the request.

We recommend that the testing technicians review test results for too few replicates and for inconsistent numbers, but **NOT** by comparing the sample standard deviation to the computerized standard deviation limits. To "review data for inconsistent numbers" is still a somewhat subjective statement which can be explained by several examples. If 14 of the 15 replicates of a physical property (Total RTD, for example) are between 35 and 40, and one result is a 90, this is an inconsistency in the data which may be a result of one cigarette being damaged or tested improperly. If approximately half of the data are between 35 and 40 and the other half are between 85 and 90, this may be due to two samples being mixed together. If the numbers consistently decrease drastically within a sample, for example from 85 to 60, this may be due to an equipment problem. An inconsistency in the data should be considered a flag to investigate for an assignable cause, not a criteria to indiscriminately reject data or recheck a sample.

If an assignable cause is determined, either as a result of detecting inconsistent data, as a result of a control chart alarm, or any other sample problem, mix-up or equipment malfunction, we recommend that the testing technicians have the authority to reject data. We further recommend that the rejected data and its cause for rejection is documented in computer notes editing. If enough data are rejected to require a recheck, the testing technicians have the authority to request a recheck, or ask the technical leader to do so depending on the procedures set forth in the laboratory. To accomplish these tasks, we recommend that the Natural Management Teams within the laboratories charter sub-teams to begin developing lists of assignable causes for each test. The sub-teams should consist of testing technicians since they are the ones closest to the process and they know the equipment and the test better than most. The lists of assignable causes would be a living document, that would grow as necessary.

In addition, a team should be assigned to develop guidelines for consistent use of the notes editing function, and to ensure that the notes editing function is available for all technicians to access during testing. This includes, but is not limited to, requesting a PC for the lucite room (where assignable causes can be detected on the TPM pads during transfer), and ensuring that the notes editing screen can be minimized on the same PC on which testing is performed in the Physical Properties laboratory. Additionally, this sub-team should investigate the computer trail for the notes editing fields to determine when notes should be captured as "lab-only", where the notes reside in the computer, and whether modifications need to be made to this function.

Certain other data handling issues can be resolved to reduce unnecessary work for the testing technicians. If a port's TPM and Puff Count data are rejected (via the "bad port" routine) due to

equipment malfunction or sample problem, the computer system should automatically set the corresponding Nicotine and Water values to "missing." Also, if a water result is negative due to detection being lower than the standard, this value should automatically be set to "0.0000."

Technical Leaders

The PTL computer system currently contains an Automatic Data Approval Program (ADAP): that is, the computer's first check of standard deviation, MAD outlier program (if necessary, based on first standard deviation check), and second standard deviation check (if gone through MAD). While it is necessary to have such a system so that not all data must be manually reviewed, some aspects of this program may be addressed in the near future to ensure that our data are being evaluated appropriately. Regardless of what changes may occur to this system, we recommend that the technical leaders only review data that have been subjected to but not approved by the ADAP. Currently, this would include any test that is listed on the Status 50 report which lists tests not approved by ADAP, and any test on the BrioQuery® To Do report which shows tests not completed due to too few measurements.

To effectively use these two reports, we recommend that all tests be performed with a minimum of three replicates so that all appropriate data can be subjected to ADAP. In addition, a small sub-team should be chartered to assess the current standard deviation limits in the ADAP system and develop a scientific algorithm for determining objective limits. The To Do report currently runs only on domestic samples. An individual should be assigned the project to adapt the program to run against all samples in all laboratories.

We recommend that the above unapproved data results are reviewed by first investigating for assignable causes. An assignable cause may be strongly suspected although it may never be unequivocally proven. For example, in analyzing a smoking group sheet, it may be obvious from the data that two or more samples were smoked in switched positions during a second run, although it may never be proven. If an assignable cause is found or suspected with strong enough evidence, the samples may be rechecked. Samples may also be rechecked if there are not enough data values, as determined by the test definition. If the standard deviation of a sample is high enough to cause it not to be approved, and no assignable cause is found, the sample may be rechecked if the standard deviation is at least twice the acceptable limit. This will confirm that the variation is due to the sample and not the testing process.

If a technical leader requests a recheck, all original data values are automatically rejected by the computer. The technical leader is to enter the reason for the recheck and assignable cause (if appropriate) into both notes editing and the laboratory's recheck notebook. We recommend that all rechecked data be subjected to ADAP but **NOT** be automatically approved by the program (this may already be the procedure but we have found situations where it has not proceeded this way). This would ensure that all rechecked data are reviewed by the technical leader to resolve the original reason for the recheck. If the reason for the recheck was high standard deviation, and the rechecked data also have a high standard deviation, unless an assignable cause is found, the data are to be approved regardless of the resulting standard deviation (no second recheck for double the standard deviation limit). The original high standard deviation is therefore confirmed to be a result of sample variation, not testing variation.

Finally, we recommend that the technical leaders review the work instructions with the testing technicians **AT LEAST** twice a year, or more frequently, as deemed necessary by laboratory technical leadership. Following each review, each testing technician is to be observed performing the procedures and their proper use of the work instruction is to be documented. Likewise, improper use of the work instruction is to be corrected and documented.

Receiving and Reporting

The sample receiving function provides the first opportunity for PTL to ensure that our samples are entered into the system correctly, tests are requested correctly and the appropriate paperwork is generated. This is the first opportunity to avoid sample mix-ups in the testing process. It is also important that the analysts accurately obtain and record as much relevant information from the collaborator as possible. Especially in the case of developmental samples, information regarding the program or project may prove useful in the final review of the request.

The receiving and reporting analysts monitor the request in process to ensure that testing is completed in a timely manner. Once testing is completed, they review the Preliminary Report and other data reports to ensure the integrity of the request prior to the release of data to the collaborator. We recommend that the following guidelines be utilized in reviewing the request:

A. **Review of Standard Deviation Warnings**

Warnings are printed on the Preliminary Report to denote test samples resulting in a standard deviation higher than the pre-determined acceptable limit. These situations should have already been reviewed at the technical leader level via the use of the Status 50 report. If so, they may have already been rechecked, either as a result of a documented assignable cause or to confirm a grossly high standard deviation (twice the acceptable limit). To assist the receiving and reporting analysts, we recommend that any recheck result printed on the Preliminary Report be flagged or identified in some way as a rechecked value. (Notes editing should also be referenced by the receiving and reporting analyst to view comments from the technical leader or testing technicians.) Since standard deviation warnings should have already been reviewed by a technical leader, we recommend that receiving and reporting analysts only review samples with standard deviations twice the acceptable limit. If a test sample still has a high standard deviation after being rechecked, this second high standard deviation confirms that the variation is due to the sample and not the process, and no further investigation is required. If a high standard deviation sample (twice the limit) has not yet been rechecked, we recommend that the receiving and reporting analysts take the following action:

1. Available Information - Assess any information obtained regarding the program or project. Special projects may indicate developmental work which could explain greater variation than usually observed. If available information explains the variation, no further action is required.

2. Investigate and/or Confirm - If there is no information to explain the sample variation, the receiving and reporting analyst should initiate investigation for

assignable cause. This should include looking for evidence of a sample mix-up, testing errors, or system errors. If an assignable cause is determined, it should be recorded in notes editing. Regardless of whether an assignable cause is determined, if sample is still available, a recheck should be initiated to either test the correct sample (in case of a mix-up), correctly test the sample (in case of a system or testing error) or confirm the sample variation (to verify that it is not due to testing variation).

B. Review of Averages

Samples received for testing in PTL may have targets set for production, historical data, both, or neither. We recommend the average test results be reviewed relative to this available information as follows:

1. Samples with Targets - If targets are available for certain test parameters, the receiving and reporting analysts should review the test averages against these targets according to the guidelines in attachment 6. This serves primarily as a check on the accuracy of the sample.

2. Samples with Historical Data - If historical data are available for the samples, the receiving and reporting analysts should review the test averages against a 3-standard deviation (historical) confidence interval around the historical average. This creates an approximation to a control chart for the sample and serves primarily as a check on the trend of the sample.

3. Samples with Both Targets and Historical Data - It is important to maintain a distinction between the guidelines used for targets and those used for trends; the target guidelines are related to production tolerances (for smoking parameters) and these tolerances can not be applied to trends. However, the results of comparing the average to the target should be used in conjunction with the results of comparing the average to the trend; the two provide different information that needs to be assimilated prior to investigation.

   Example - If a tar average "fails" the target comparison test, the tar value may be within the historical 3-standard deviation confidence interval, but results have been steadily dropping. Therefore, the test average is justifiable and the deviation from target should be considered a product problem. However, if a test average "fails" the target comparison test, does not fall within the 3-standard deviation limit, and the data have not been trending toward this value, there may have been a sample or testing problem in PTL.

4. Samples with Neither Targets nor Historical Data (developmental, etc.) - If a sample parameter has no target and no historical data, the averages may be assessed based on information from the collaborator. Special programs or projects may include certain models with loose targets for testing parameters.

C. **Confirmation of Averages**

If reviews of test averages result in outcomes that are questionable, we recommend that the receiving and reporting analysts take the following steps:

1. Determine if relationships between test parameters confirm the test averages.

2. Determine if available information from the collaborator regarding the program or project confirm the test results.

3. Determine if the test results have already been rechecked which would serve as a confirmation of the results.

4. Determine if an assignable cause can be found (sample mix-up, system or testing error). If found, and enough sample remains, a recheck should be initiated.

5. If none of the above steps verify the average, and a recheck has not yet been performed but enough sample remains to do so, a recheck should be initiated to ensure that we have correctly tested the correct sample. Additionally, appropriate documentation needs to be recorded in notes editing.

6. If appropriate, the collaborator should be contacted to discuss the discrepancy in the results.

Specific Tasks

Attachment 7 outlines the specific tasks that need to be accomplished in order to put all the recommendations in place. Each task has been prioritized and is assigned either an individual or group that this team recommends be chartered to complete it. The priorities were assigned based on a combination of how much effort we feel the task should require and how important the result is. The first six items are prioritized with an "*" because we feel that, if accepted, these items require so little effort on the part of PTL employees that they should be pursued irrespective of the other items. Each line-item also contains an estimate of how long we feel it should take to complete.

If you have any further questions, please feel free to contact any one of us.

Attachments

Distribution:
Liz Chambers
Gloria Hicks-White
Wade Mokarry
Ken Podraza
Brenda Strang

CC:
Charlene Callicutt
Becky Tobey